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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SINGH, ANOOP KUMAR	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 06/06/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/602,441	MAJUMDAR ET AL.	
	Examiner	Art Unit	
	Anoop Singh	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/905*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The Examiner prosecuting this application has been changed. Any inquiries relating to the examination of the application should be directed to Examiner Singh. The telephone number is provided at the end of this office action.

2. Applicants' amendment filed April 13, 2006 has been received and entered. Claims 13-15 have been amended. Claims 1-24 are pending.

Election/Restrictions

3. Applicant's election without traverse of the invention of group II (claims 13-24, nucleic acid composition) filed April 13, 2006 is acknowledged. However, Applicants traversed the requirement of election between composition and methods. Applicants' argument of examining method for eliciting an immune response with the elected group comprising plurality of polynucleotide composition was found persuasive. Applicant's also traverse the requirement of election of one TERT sequence. Applicant's argument of examining other sequences with elected Sequence ID 4 was found not persuasive, as each of these sequences have distinct structure as stated in previous office action. Applicants also elected GM-CSF as specie for immunization promoting factor.

The requirement is still deemed proper and is therefore made FINAL.

4. Claims 1-24, directed to polypeptide composition and a method of using polypeptide are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on April 13, 2006.

Claims 1-24 are under consideration as drawn to a nucleic acid composition and a method for eliciting an immune response in a mammalian subject that is specific for its own telomerase reverse transcriptase (TERT) comprising administering to the subject composition of nucleic acid encoding TERT.

5. Claims 1-24 are under consideration.

Claim Objections

6. Claims 1-24 are objected to because of the following informalities: Claims1-24 continue to recite in part to subject matter that is withdrawn and therefore, instant claims should be rewritten to recite elected invention. However, for purposes of compact prosecution, claims 1-24 will be treated as if dependent on a composition directed to nucleic acid. Appropriate correction is required.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-12 and 15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for eliciting an immune response in a mammalian subject that is specific for its own telomerase reverse transcriptase (TERT), comprising administering to the subject an immunogenic composition comprising a nucleic acid encoding a protein with at least 20 consecutive amino acids of TERT of another mammalian species does not reasonably provide enablement for a method comprising immunogenic composition and GMCSF or any other pharmaceutical composition intended for the treatment of cancer. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claim 1 is directed to a method for eliciting an immune response in a mammalian subject that is specific for its own TERT by administering to the subject an immunogenic composition containing a nucleic acid encoding a protein with at least 20 consecutive amino acids of TERT. Claim 2 limits the protein of method of claim 1 to include at least 100 consecutive amino acids of TERT of the other mammalian species. Claim 3 limits the method of claim 1 to include at least four times administrating the nucleic acid to the subject. Claim 4 further comprises a subsequent administration of a second composition containing a second nucleic acid encoding protein with at least 20 consecutive amino acids of TERT of the same species as the subject. Claim 5 limits the immune response to include a cytotoxic T cell response. Claim 6 limits the protein to include full-length

TERT. Claim 7 limits the method of claim 1 to include increase telomerase activity in cells surrounding the site of administration of immunogenic composition. Claim 8 limits the method of claim 1 to include the protein lacks telomerase activity when associated with telomerase RNA due to one or more changes in amino acid sequence. Claim 9 limits the composition in method of claim 1 to include either plurality of nucleic acids encoding plurality of different proteins, each comprising at least 20 consecutive amino acids of TERT from one or more mammalian species different from the mammalian subject to which the composition is administered. Claims 10-11 limit the protein of claim 1 to SEQ. ID NOs:4 the composition containing an adenovirus expression vector encoding the protein respectively. Claim 12 includes a factor selected from IL-12, GM-CSF, IL-2 and MPL in the composition of claim 1. It is noted that claims 15 is directed to a pharmaceutical composition that is intended for the treatment of cancer.

In determining whether Applicant's claims are enabled, it must be found that one of skill in the art at the time of invention by applicant would not have had to perform "undue experimentation" to make and/or use the invention claimed. Such a determination is not a simple factual consideration, but is a conclusion reached by weighing at least eight factors as set forth in In re Wands, 858 F.2d at 737, 8 USPQ 1400, 2d at 1404. Such factors are: (1) The breadth of the claims; (2) The nature of the invention; (3) The state of the art; (4) The level of one of ordinary skill in the art; (5) The level of predictability in the art; (6) The amount of direction and guidance provided by Applicant; (7) The existence of working examples; and (8) The quantity of experimentation needed to make and/or use the invention.

These factors will be analyzed, in turn, to demonstrate that one of ordinary skill in the art would have had to perform "undue experimentation" to make and/or use the invention and therefore, applicant's claims are not enabled.

Furthermore, USPTO does not have laboratory facilities to test if an invention will function as claimed when working example are not disclosed in the specification, therefore enablement issues are raised and discussed based on the state of knowledge pertinent to an art at the time of the invention, therefore, skepticism raised in enablement rejections are those raised in the art by artisan of expertise.

The aspects considered broad are: a pharmaceutical composition of nucleic acid containing xenogeneic epitopes of TERT in conjunction with factors such as GM-CSF for the intended use in cancer therapy. It is noted that as instantly recited, claimed invention reads on broad genera of DNA vaccine by delivering via any vector to elicit immune response, and delivery of DNA is generally not enabling in humans due to problems with, *inter alia*, targeting and expression of transgenes at effective level by any vector or other delivery vehicle to elicit therapeutic effective immune response for the treatment of any cancer. The specification fails to provide an enabling disclosure for the claimed invention because the specification fails to provide sufficient guidance as to (i) how an artisan of skill would have practiced the claimed method in treating any form of cancer by administering via any route and expressing plurality of DNA vaccine containing xenogeneic epitopes of TERT, (ii) the claimed method would have resulted in immune response sufficient to treat any form of cancer. An artisan would have to carry out extensive experimentation to make and use the invention, and such experimentation

would have been undue because art of gene delivery *in vivo* is unpredictable and specification fails to provide any guidance as to how the claimed method would have been practiced in any subject. As will be shown below, these broad aspects were not enabled for the claimed invention at the time of filing of this application because neither the specification nor the art of record taught sufficient guidance to practice the claimed invention. For purposes to be shown in the state of the prior art, the question of lack of enablement is discussed.

As a first issue, the claim 1-12 embrace a method for eliciting an immune response in a mammalian subject that is specific for its own TERT by administering to the subject an immunogenic composition containing a nucleic acid encoding a protein with at least 20 consecutive amino acids of TERT of another mammalian species. Subsequent claims limit the composition to contain xenogeneic epitopes of TERT. The specification also teaches that homologs are full-length TERT and TERT fragments of various lengths of species xenogeneic to the subject being treated. Furthermore, it is also noted that Applicants also contemplate using naturally occurring TERT sequences modified with one or more amino acid changes introduced for any reason (pp 3, para 4). Thus, scope of instant claim also encompasses an isolated nucleic acid molecule encoding a telomerase reverse transcriptase protein from different mammalian species. However, specification fails to provide an enabling disclosure for the full scope of the claimed nucleic acid sequence The specification teaches an alignment of TERT encoding gene and protein sequences from human (SEQ. ID NO: 1), mouse (SEQ. ID NO: 3), hamster (SEQ. ID NO:5), rat (SEQ. ID NO:7), and dog (SEQ. ID NO:9) (Figure 9

and 10). However, it is art recognized that even conservative amino acid substitutions can adversely affect proper folding and biological activity if amino acids that are critical for such functions are substituted, and the relationship between the sequence of a polypeptide and its tertiary structure is neither well understood nor predictable. The xenogenic variants as claimed are simply consensus sequence without any biological function. The mere identification of critical regions would not be sufficient, as the ordinary artisan would immediately recognize that the encoded polypeptide must assume the proper three-dimensional configuration to be active, which is dependent upon the surrounding residues (see Ngo, in The Protein Folding Problem and Tertiary Structure Prediction, Merz et al. (eds.), Birkhauser Boston: Boston, MA, pp. 433 and 492-495, 1994. Rudinger in Peptide Hormones, Parsons (ed.), University Park Press: Baltimore, MD, pp. 1-7, 1976, Guo et al, PNAS 101425): 9205-9210, 2004). Although specification provides evidence that immunization with hTERT generates CTLs that are specific for the mouse TERT expressed endogenously by the B16F10 tumor and human TERT imparts cytotoxic immunity against endogenously expressed antigen expressed by tumor cells (pp 13, lines 23-35 bridging to pp 14, lines 1-4 and Figure 3 A and B). The specification does not provide any working evidence to suggest that any other xenogenic composition or naturally, occurring TERT sequences modified with one or more amino acid changes introduced would elicit an effective immune response. Thus, it is apparent that an artisan would have to carry out extensive experimentation to make and use the invention, and such experimentation would require undue experimentation

to practice method as claimed because only nucleic acid encoding optimal protein folding would have provided effective immune response sufficient to regress tumor load.

As a second issue, claim 12 limits the method of claim 1 to include plurality of immunostimulant as adjuvant, while claim 15 recite a combination of pharmaceutical compositions for eliciting an immune response. In view of disclosure, working example and recitation of intended use in composition claims, it is evident that inclusion of adjunct or recitation of pharmaceutical composition is intended to elicit greater immune response for the treatment of cancer. It is known in the art that the goal of tumor vaccination in the induction of tumor immunity is to prevent tumor recurrence and to eliminate residual disease. However, Ezzell (J NIH Res., 1995, 7, 46-49) reviews the current thinking in cancer vaccine and states that tumor immunologists are reluctant to place bets on which cancer vaccine will prove effective in the long run (see the entire document, particularly last paragraph) and further states that no one is very optimistic any molecule could trigger an immune response strong enough to eradicate tumors or even to prevent the late growth of micro metastases among patients whose tumors have been surgically removed or killed by radiation or chemotherapy (pp 48, para 6). While the specification teaches hTERT in combination with mTERT enhances CTL in a mouse model, however, it does not teaches specific information required by the Artisan to reasonably predict that any xenogenic or naturally occurring variant of TERT of any non human mammalian species could be used as xenogenic epitopes for the treatment of cancer by eliciting an immune response that is effective for long enough for sustained period of time that would have beneficial effects in treating any form of cancer in

humans. In addition, Srinivasan et al describe that the hallmarks of a successful vaccine are judged by multiple endpoints, with the most important one being control of dissemination of tumor. There are several steps involved in the generation of anti-tumor immune responses. Srinivasan while presenting positive outlook of xenogeneic approach also describe that " ultimately an adaptive response should be generated to control antigen escape variants. The potency of the response, once induced, must be increased to the magnitude of that as found in infectious disease settings. A break anywhere in this sequence can give rise to disease progression. Unfortunately, this frustration is frequently encountered. Specific immune responses to tumor antigens *in vitro* can be detected in patients undergoing various immuno therapies that do not translate to a desired clinical response". In the instant case, specification teaches that a significant delay (emphasis added) in tumor growth was observed in mice receiving Adh TERT vaccination compared with mice receiving control virus. However, the data presented in Figure 8 shows a significant regression of tumor growth only at day 29 (pp 15 of the specification). It is noted that there was no significant difference in the regression of tumor growth prior to 27 days in an immunization protocol. The survival graph by the Kaplan-Meier method that is a logrank test designed to test the difference between two survival curves would have provided better indication of any potential benefit of AdhTERT. Further, it is not apparent from this study whether instant composition would show any efficacy in a therapeutic protocol wherein mice is immunized after tumor cells are inoculated. It is apparent that an artisan would have to perform undue experimentation that are not routine rather critical for the successful

outcome of any cancer therapy. Amending the claims to recite an immunogenic composition instead of pharmaceutical composition would obviate his part of instant rejection under 112, first paragraph.

In conclusion, in view of breadth of the claims and absence of a strong showing by Applicant, in the way of specific guidance and direction, and/or working examples demonstrating the same, such invention as claimed by Applicant is not enabled for the claimed inventions. The specification and prior art do not teach a method of *in vivo* delivery of DNA vaccine such that it render any subject sufficiently to elicit a immune response for a sustained duration for the prevention or treatment of cancer of any etiology and pathology. An artisan of skill would require undue experimentation to practice the method as claimed because the art of DNA vaccine and *in vivo* delivery and treatment of cancer in general by recombinant vaccine containing xenogeneic epitope of TERT *in vivo* was unpredictable at the time of filing of this application as supported by the observations in the art record.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 13-21 and 23-24 are rejected under 35 U.S.C. 102(b) as being anticipated by Morin et al (WO 99/27113, dated 6/3/1999, IDS).

Morin et al teach a composition of mouse TERT that has a 100% sequence identity to SEQ ID NO: 4 of the instant application (mouse TERT). Furthermore, sequence disclosed by Morin et al encompass a nucleic acid encoding protein containing at least 20, 100 consecutive as well as full-length amino acids of mouse TERT (Sequence search and Figure). It is noted that Morin et al also contemplate using suitable buffer for multiple purposes. In addition, Morin et al teach the sequence alignment of mouse TERT with human TERT. Therefore, a combination of pharmaceutical composition comprising mTERT and hTERT is also anticipated by the teaching of Morin. Further, Morin contemplates an mouse TERT and telomerase enzyme that have been modified in site specific manner to modify or delete any or all function of telomerase enzyme or mTERT protein (pp 46, lines 17-19). The art further teaches that mTERT of the invention is capable of catalyzing the synthesis of telomeres when associated with RNA moiety (pp 87, lines 9-14, pp 13, lines 7-10). In addition, Morin teaches a number of vectors including adenoviral vector for introducing mTERT into the cells to produce a cell that produces a desirable protein (pp 40, lines 33-34 bridging to pp 41, lines 1-8). The disclosure also provides a kit for detection of mouse TERT gene comprising a container containing a molecule that can be a mTERT nucleic acid (pp 8, cline 3-5). It is emphasized that packaging and instruction of use is inherent in the kit disclosed by Morin.

Therefore, a composition comprising a nucleic acid encoding mouse TERT as disclosed in prior art is inherently capable of generating an immune response upon administration in any subject to have a desirable effect on the subject.

Accordingly, Morin et al anticipate claims 13-21 and 23-24.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

12. Claims 13 and 22-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Morin et al (WO 99/27113, dated 6/3/1999, IDS) and Chen et al (US Patent publication number 20030143228, dated 7/31/2003, effective filing date 10/29/2001).

Morin et al teach a composition of mouse TERT that has a 100% sequence identity to SEQ ID NO: 4 of the instant application (mouse TERT). Furthermore, sequence disclosed by Morin et al encompass a nucleic acid encoding protein

containing at least 20, 100 consecutive as well as full-length amino acids of mouse TERT (Sequence search and Figure). It is noted that Morin et al also contemplate using suitable buffer for multiple purposes. In addition, Morin et al teach the sequence alignment of mouse TERT with human TERT. Therefore, a combination of pharmaceutical composition comprising mTERT and hTERT is also anticipated by the teaching of Morin. Further, Morin contemplates an mouse TERT and telomerase enzyme that have been modified in site specific manner to modify or delete any or all function of telomerase enzyme or mTERT protein (pp 46, lines 17-19). The art further teaches that mTERT of the invention is capable of catalyzing the synthesis of telomeres when associated with RNA moiety (pp 87, lines 9-14, pp 13, lines 7-10). In addition, Morin teaches a number of vectors including adenoviral vector for introducing mTERT into the cells to produce a cell that produces a desirable protein (pp 40, lines 33-34 bridging to pp 41, lines 1-8). The disclosure also provides a kit for detection of mouse TERT gene comprising a container containing a molecule that can be an mTERT nucleic acid (pp 8, cline 3-5). However, Morin et al do not explicitly teach a composition comprising nucleic acid encoding plurality of protein from one or more non-human mammal.

At the time of invention, Chen et al teach identification of hTERT-restricted epitopes and the use of these identified epitopes to elicit an immune response against the epitope. Chen et al teach various method of creating variants of hTERT including domain switching that involves the generation of chimeric molecules. It is noted that Chen et al contemplate comparing various hTERT proteins to make predictions as to

the functionally significant regions of these molecules. It is possible, then, to switch related domains of these molecules in an effort to determine the criticality of these regions to hTERT function. Chen et al also teach fusions protein including linking of functional domains, such as active sites from enzymes, glycosylation domains, cellular targeting signals or transmembrane regions. Thus, Chen et al teach a composition of hTERT comprising various functional domain of hTERT. The studies of Chen et al is directed at the use of the hTERT polynucleotide sequences to treat subjects with hyperproliferative diseases including various form of cancer by delivering the composition containing an adenoviral expression vector encoding hTERT. It is noted that Chen et al also teach that immunogenicity of a particular immunogen composition can be enhanced by the use of adjuvant including IL-2, IL-12, and GMCSP. However, Chen et al do not disclose using non-mammalian TERT for eliciting immune response.

It would have been obvious for one of ordinary skill in the art at the time of invention to modify the nucleic acid composition described by Morin to also include other functional domains of TERT as taught by Chen et al to elicit better immune response of recombinant nucleic acid sequence encoding modified protein. Chen et al provided the motivation to modify the composition of mouse TERT sequence to include other functional variants of TERT because one could study the role of TERT fusion protein or multiple domains of TERT in eliciting immune response. In addition, Artisan would have been further motivated to include an adjuvant such as IL-2, IL-12, and GMCSP with the composition to increase the immune response as suggested by Chen.

One who would practiced the invention would have had reasonable expectation of success because Chen et al had already disclosed a composition of hTERT comprising a polynucleotide encoding hRERT protein that is modified to include other domains for eliciting efficient immune response. An artisan of ordinary skills would have been motivated to use nucleic acid encoded by mTERT disclosed by Morin to further optimize for other variants of mTERT because prior art suggested that Variants of TERT preparation is effective (Chen et al) in eliciting immune response. One of ordinary skill in art would have been motivated to combine the teaching of Morin and Chen because a composition comprising mTERT or plurality of different mTERT would have been provided information of different domains of mTERT for eliciting immune response in a mammalian subject for the treatment of variety of disease.

Therefore, the claimed invention would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention.

13. Claims 1-13 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chen et al (US Patent publication number 20030143228, dated 7/31/2003, effective filing date 10/29/2001), and Morin et al (WO 99/27113, dated 6/3/1999, IDS) and further in view of Tian et al (Progress in Natural Science, 2001, 11(12), pp 893-904)

The combined teaching of Chen and Morin have been discussed above. However, none of the reference teaches a method of eliciting an immune response after administering xenogeneic composition.

Tian et al teach the role of xenogeneic homologous genes in cancer therapy. Tian teaches a number of xenogeneic homologous genes that are well conserved and they show the structural and/or functional similarity between various species to some degree. The nucleotide changes between various xenogeneic homologous genes are derived from mutation, and most of them are neutral mutations. Tian et al teach that subtle differences in xenogeneic homologous genes can break immune tolerance, enhance the immunogenicity and induce autologous immune response to eliminate tumor cells (abstract).

It would have been obvious for one of ordinary skill in the art at the time of invention to modify the method of eliciting immune response taught by Chen et al to include composition of nucleic acid encoding mouse TERT as disclosed by Morin. An Artisan would be motivated to first adminster mTERT in a human subject because Tian had already described the importance of xenogeneic homologous genes in cancer therapy. Morin et al provided the motivation by providing the sequence comparison between the two species and Tian had already taught that slight differences in xenogeneic homologous genes could break immune tolerance, enhance the immunogenicity and induce autologous immune response to eliminate tumor cells.

One who would practiced the invention would have had reasonable expectation of success because Chen et al had already shown an effective immune response by administering hTERT composition and use of other TERT with various adjuvant to generate immune response has been routine in the art at the time of the instant invention was made. An artisan of ordinary skills would have been motivated to use

polynucleotide encoded by the sequence disclosed by Morin because prior art suggested that homologous xenogeneic gene is effective (Tian et al) in eliciting immune response. One of ordinary skill in art would have been motivated to combine the teaching of Chen, Morin and Tian because a method for eliciting immune response by administering mTERT in a mammalian subject or plurality of xenogeneic homologous TERT would have inhibited the immune tolerance, enhanced the immunogenicity and induced autologous immune response to eliminate tumor cells.

Therefore, the claimed invention would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention

14. No Claims allowed.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anoop Singh whose telephone number is (571) 272-3306. The examiner can normally be reached on 9:00AM-5:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272- 0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Anoop Singh, Ph.D.
Examiner, AU 1632